COMMENTARY

Do Patent Terms Impact Domestic R&D Spending in the Pharmaceutical Industry?

Les durées des brevets ont-elles une incidence sur les dépenses nationales en R&D dans l'industrie pharmaceutique?

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Abstract

Grootendorst and Di Matteo's study showed that extended patent terms in Canada significantly increased domestic R&D spending in the pharmaceutical industry. However, some of the authors' assumptions and methods, including the choice of control variables, the technique used in calculating policy impacts over time and the failure to incorporate the influence of global factors, are problematic. The overall impression is that the study highlights a correlation between extended patent terms and increased R&D expenditure in Canada but does not provide firm evidence of a causal link.

Résumé

L'étude de Grootendorst et de Di Matteo a révélé que la prolongation des brevets au Canada a fait augmenter de manière significative les dépenses nationales en R&D dans l'industrie pharmaceutique. Des observateurs ont remis en cause certaines des hypothèses et des méthodes utilisées par les auteurs, y compris le choix des variables de contrôle, la méthode employée pour calculer l'incidence des politiques avec le temps et la non-considération de l'influence des facteurs mondiaux. L'impression générale est que l'étude met en évidence une corrélation entre la prolongation des durées des brevets et une augmentation des dépenses en R&D au Canada, mais ne fournit pas de preuves solides quant à l'existence d'un lien causal.

Grootendorst and Di Matteo analyze the net effects of extended pharmaceutical patent terms on domestic pharmaceutical R&D expenditures and pharmaceutical spending between 1988 and 2002, taking into account the mitigating effects of price controls and the retrenchment of public prescription drug subsidy programs. They find that the policy changes were indeed associated with substantially increased domestic R&D spending in the pharmaceutical sector of around $4 billion. The authors also calculate the resulting per capita increased life expectancy value of this additional expenditure.

This is a complex area to research because of the difficulties of adequately isolating the impact of legislation as distinct from other external influences on R&D expenditure, and the problem of how to place economic value on the individual and social benefits of pharmaceutical R&D. The authors acknowledge that their analysis is not a fully comprehensive one, and clearly set out the limitations of the study, which on the whole is well argued. However, some of their assumptions are rather simplistic, particularly when extrapolating R&D expenditure to an assessment of overall value for Canada. Moreover, the methodology used to calculate expenditure appears questionable in several areas, and there are a few inaccuracies that may have affected the analysis and its outcomes. There are also some definitional inconsistencies that may have a bearing on the efficacy of the analyses. For example, R&D is defined differently between Statistics Canada and the Patented Medicine Prices Review Board, while data from the Canadian Institute of Health Information (CIHI) include some non-drug costs.

These points are important, because reliability of the results hinges on the assumptions made and the indicators chosen for use in measuring costs and benefits. The overall impression is that the study highlights a correlation between extended patent terms and increased R&D expenditure in Canada, but it does not provide real evidence of a causal link.

Problematic assumptions also relate to the choice of control variables. First, the use of the United States as a comparison country with only recently lengthened patent terms seems misguided. There are also major differences between Canada and the United States in terms of the time it takes to approve patents; these differences complicate the comparative analysis of impacts over time. Second, in assessing what would have happened to R&D in the absence of patent restoration, the validity of using the motor vehicle industry as a control is highly questionable. The motor vehicle industry is much less dependent on patent protection than the pharmaceutical industry, and investment in R&D in the Canadian motor vehicle industry has been artificially inflated by the Auto Pact agreement with the United States. It is somewhat puzzling that the authors did not select an industry subject to similar patent regulations as the pharmaceuticals industry, such as the software industry.

There are also potential weaknesses in the analysis regarding the way that impacts over time are calculated. In general, there is a significant time lag between R&D investment and the realization of quantifiable benefits, a disparity that suggests the 14-year time frame for this study may be inadequate. It can take up to 20 years from the initial development of the research infrastructure to the realization of commercial benefits of new drugs. Even if the research capacity already exists, it generally takes at least 10 years for a new product to reach the market, so realistically the benefits from new molecular entities (NMEs) produced from 1988 onwards would not be realized until at least the late 1990s.

Moreover, as Joel Lexchin of the Faculty of Health at York University has pointed out (J. Lexchin, personal communication, September 2006), overall sales of many drugs are generally lower at 10–12 years into their life cycle, when generics are now introduced, compared with five to seven years into their life cycle, when generics were introduced prior to 1987. As a result, the potential savings are lower. As Grootendorst and Di Matteo note in their paper, one of the main reasons for the increase in drug expenditures in Canada is the substitution of newer, more expensive drugs for older ones. If compulsory licensing were still in existence, there would be generic competition for these more expensive drugs about four to six years earlier than is now the case.

Lexchin also argues that the monopoly sales period would be more accurately calculated as 11 years rather than the 10 years used by the authors in their calculations, owing to a decrease over time in patent approval times.[1] Others, on the other hand, have suggested that a slowdown in provincial reimbursement of innovative medicines has added more than a year to listing times.

Furthermore, with its focus on domestic drug spending and R&D expenditure, this study seems to underestimate the extent to which the Canadian pharmaceuticals industry is affected by international influences. The global nature of the pharmaceuticals industry makes it very difficult to establish a relationship between domestic

policies and R&D expenditure, since decisions regarding R&D activity are often taken at a global headquarters level and are influenced by many factors other than patent terms. So, for example, some have suggested that the availability of research expertise in countries such as India is a key variable contributing to an increase in generic R&D. Additionally, the authors' assumption that R&D spending would have remained at 6% in the absence of extended patents and increased drug costs does not take account of the possible impact of external factors, such as the increasingly competitive nature of global pharmaceutical R&D.

Moreover, it is extremely unlikely that the domestic R&D environment would be capable of producing four to six NMEs independently, that an additional $4–6 billion invested in R&D would result in drugs launched solely out of Canada, or that they would be developed exclusively for the small Canadian market. It is much more likely that the drugs would be developed with global collaboration and for a world market, with the overall costs and benefits to Canada being much more difficult to estimate.

There is also a need to consider the specific relationship between R&D input and level of benefits, as it can by no means be assumed that a certain level of investment can be equated to particular levels of output. The type of R&D being carried out should also be taken into account when measuring outputs and benefits. Federal and provincial governments intentionally invest in "basic research," which often has no immediate practical application, yet important new discoveries are often made in this field of research. Some have also questioned the value of R&D that is focused only on copying molecules and doing bioequivalency studies compared to, for example, conducting clinical trials – an area of difference in the R&D focus of generic versus brand-name companies, with the latter concentrating more on clinical trials in Canada.

Perhaps one of the major problems is that the pharmaceutical industry does not lend itself easily to macro-analysis, as there are big differences between different types of drugs and their relative values that considerably complicate the relationship between R&D inputs and outcomes. Not only are there different pricing structures and usage patterns for prescription medicines, over-the-counter drugs, and generic and brand drugs, for example, but there are changes over time in the uses of different drugs, increases in the efficacy of some drugs and differences in side effects, all of which need to be quantified. It might also be argued that the increasing efficacy of drugs may have a ripple effect in the sense that it keeps people alive longer and therefore drives up drug costs, or alternatively that increasing drug use may be damaging to health. Moreover, it can't necessarily be assumed that all NMEs represent significantly increased value in terms of therapeutic advance, since this varies among drugs and over time. Neither should it be assumed, as Grant Perry, Director, Federal Affairs and Reimbursement at GlaxoSmithKline has noted (G. Perry, personal communication, November 2006), that later entrants into a therapeutic class are necessarily of lower value. In any case, there is likely to be considerable spin-off value from R&D invest-

ment, in terms of research capacity, knowledge generation and more, whether or not NMEs are actually produced. It would be helpful to see a measure of spin-off value included in the analysis.

Although the authors do attempt to control for demographic factors, the results might be more accurate if they also incorporated the effects of population change over time, since this is likely to have a major impact on drug use and expenditure. Provincial-level analyses would also likely produce more meaningful results, as there will be considerable variations in the costs and benefits of R&D spending among different provinces, particularly given provincial controls on drug costs.

According to Lexchin, the proportion of total sales devoted to R&D in Canada has declined significantly since 2002 and now stands at 8.8%, while total prescription drug spending has continued to increase. Perry, on the other hand, notes that R&D investment has continued to rise in dollar terms, but that Canada's position in global R&D markets has declined due to increasing competition. Clearly, there are a range of factors involved, and the results of this analysis cannot therefore be assumed to apply to the current situation regarding pharmaceutical R&D and its value to Canada.

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NOTES

1. Back in 1993, Canada's Research-Based Pharmaceutical Companies (Rx&D) was claiming that there was 10 years of effective patent protection (J. Lexchin, personal communication, September 2006). In 1993, drug approval times were 1,044 days compared to 717 days in 2001, or almost a year longer. Somehow, the decrease of a year did not get reflected in the patent life that Rx&D presented. It might be postulated that the one-year gain in approval time was taken up by longer clinical testing times, but that does not seem to be the case. At most, times from the start of clinical testing to the filing of a submission for approval have increased by 3.5 months during the 1990s. In the United States, effective patent life for selected drugs is between 13.9–15.4 years. Some of that time is accounted for by provisions not available in Canada (patent term restoration = 2.3 years, paediatric exclusivity = 0.5 years), and approval times are about 0.8 years faster in the United States. Using these figures, Canadian effective patent times should be 10.3–11.8 years, a number roughly consistent with the calculation based on shorter approval times.